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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/992,680	11/19/2001	Chi-Huey Wong	84503	1046

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EXAMINER

PRATS, FRANCISCO CHANDLER

ART UNIT PAPER NUMBER

1651

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

### Application No.

09/992,680

### Applicant(s)

WONG ET AL.

### Examiner

Francisco C Prats

### Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 19 May 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 21-26, 28, 29 and 52-57 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21-26, 28, 29 and 52-57 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_.

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#### **DETAILED ACTION**

The amendment filed May 19, 2004, has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 21-26, 28, 29 and 52-57 are pending and are examined on the merits.

#### ***Claim Rejections - 35 USC § 103***

Claims 21-23, 25, 52, 54 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergh et al (U.S. Pat. 4,925,796) in view of Schachter et al (Methods Enzymol. 28:285-287 (1972)).

Bergh discloses compositions comprising a fucosyltransferase and GDP, for use in fucosylation of oligosaccharide moieties of glycoproteins. See column 18, lines 33-68; see also claim 25 at column 26. Bergh differs from the cited claims in failing to include the claimed GDP-fucose forming enzymes, fucose kinase and GDP-pyrophosphorylase, in his composition. However, Schachter clearly discloses that the GDP-fucose required in the fucosylation process of Bergh can be prepared using the very enzymes recited in the claims. Note the presence of both GDP and GTP in the reaction milieu of

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Schachter, as evidenced by the reaction equilibrium equation on page 285. Thus, solely looking to the cited prior art, the artisan of ordinary skill would have been motivated to have combined the fucosyltransferase of Bergh with the enzymes and substrates of Schachter so as to generate the GDP-fucose required for Bergh's fucosylation process. A holding of obviousness is therefore required.

Claims 21-25, 52, and 54, 55 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergh et al (U.S. Pat. 4,925,796) in view of Schachter et al (Methods Enzymol. 28:285-287 (1972)), as applied to claims 21-23, 25, 52, 54 and 56 above, and in further view of Demain et al (U.S. Pat. 4,178,210).

As discussed above, when taken in light of Schachter, Bergh renders obvious the compositions recited in claims 21-23, 25, 52, 54 and 56. Neither Bergh nor Schachter discloses the presence of pyruvate kinase in their compositions as recited in claim 24. However, in view of the fact that Schachter's process requires ATP, the artisan of ordinary skill would have considered the use of the well-known PEP/pyruvate kinase ATP regeneration system an obvious method of regenerating the ATP required for the ultimate synthesis of the GDP-fucose required

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in Bergh's fucosylation process. See, e.g., Demain at column 4, lines 23-26 ("[t]he preferred phosphate donor is phosphoenolpyruvate and its corresponding phosphotransferase enzyme, pyruvate kinase.") Thus, the claimed use of pyruvate kinase in an enzymatic system known to require ATP must be considered obvious.

Claims 21-26, 28, 29 and 52-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergh et al (U.S. Pat. 4,925,796) in view of Schachter et al (Methods Enzymol. 28:285-287 (1972)) and Demain et al (U.S. Pat. 4,178,210), as applied to claims 21-25, 52, and 54, 55 and 57, above, and in further view of Yamamoto et al (Agric. Biol. Chem. 48(3):823-824 (1984)).

As discussed above, when taken in light of Schachter and Demain, Bergh renders obvious the process recited in claims 21-25, 52, and 54, 55 and 57. None of Schachter, Demain or Bergh discloses the presence of an NADPH regenerating system as recited in claim 26, or the *in situ* generation of GDP mannose via the components recited in claims 28, 29 and 56. However, Yamamoto clearly discloses that compositions comprising the claimed ingredients, including the NADPH regenerating system (right column, page 283, lines 18-21), result in the production

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of GDP-fucose from GDP-mannose. Moreover, Yamamoto discloses that the GDP-fucose so synthesized is suitable for use as a fucosyltransferase substrate. See first sentence page 285. Thus, the artisan of ordinary skill, recognizing that the GDP-fucose required in Bergh's process was suitably prepared using either Yamamoto's or Bergh's system, would have been motivated to have included the enzymes required for said syntheses in Bergh's fucosylation compositions. Moreover, the inclusion of a pyruvate kinase/PEP system in such a composition would have been obvious in view of the requirement for GTP in the synthesis of the GDP-mannose used by Yamamoto's system.

In sum, the claims recite an assembly of the enzymes known in the prior art to be useful in the synthesis of fucosylated oligosaccharides. The artisan of ordinary skill, recognizing solely from the prior art that the claimed combinations of enzymes were suitable in the preparation of fucosylated oligosaccharides, clearly would have been motivated to have assembled the claimed ingredients into a single composition. Absent some demonstration of an unexpected result coming from the claimed combination, a holding of obviousness is clearly required.

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***Response to Arguments***

All of applicant's argument has been fully considered but is not persuasive of error. Regarding the alleged lack of motivation for combining the Bergh and Schachter references, and the alleged teaching away by Schachter, it is respectfully pointed out that the GDP fucose used in Bergh's fucose transfer process must be prepared somehow. One practicing the fucose transfer process of Bergh clearly would have recognized that, by including Schachter's enzymes in the fucosyl transferase medium, the substrate of the fucosyltransferase would have been produced *in situ*, thereby allowing the desired fucosyl transfer reaction to occur. As to the alleged uncertainty with respect to the interference between the two enzymes, note specifically that GDP-fucose is continually synthesized by physiologically "normal" cells containing numerous other enzymes, none of which interfere with each other to block the synthesis. Absent some direct evidence that the artisan of ordinary skill would have expected the claimed enzymes to interfere with each other, there is nothing on the record, or in the prior art, suggesting that the artisan of ordinary skill would not have reasonably expected that combining the enzymes of Schachter and Bergh would have resulted in the fucosylation disclosed by Bergh. Lastly, as to the requirement of a catalytic amount of the enzymes, it is

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respectfully pointed out that the enzymes described in the references in fact catalyze the described reactions. The limitation requiring a catalytic amount is clearly met.

With respect to the relevance of the Demain reference, note specifically that claim 24 requires the presence of a pyruvate kinase. In order to synthesize GDP-fucose by Schachter's methods, one must have ATP. See page 285 of Schachter. It is well known in the art that, in ATP-requiring enzymatic syntheses, ATP can be generated *in situ* by addition of pyruvate kinase and PEP to the reaction milieu. See Demain at column 4, lines 23-26 ("[t]he preferred phosphate donor is phosphoenolpyruvate and its corresponding phosphotransferase enzyme, pyruvate kinase.") Thus, Demain is clearly relevant because it demonstrates that one of ordinary skill preparing GDP-fucose for use in a fucosyltransferase reaction would have recognized that the claimed pyruvate kinase was required to generate the ATP required to make the GDP-fucose substrate.

With respect to the Yamamoto and Schachter disclosures and the alleged misquotations of those reference, it is respectfully pointed out that Yamamoto and Schachter are two and three pages long respectively, and that neither reference was actually quoted. Of note, applicant clearly admits (response of May 19, 2004, page 11) that the combined disclosures of Schachter and



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Yamamoto disclose all of the enzymes and constituents recited in the claims under examination.

It is noted that, by themselves, neither Schachter nor Yamamoto discloses all of the claimed limitations. However, the fact that the claimed combination was never made before applicant's filing date simply cannot, from a logical or legal standpoint, demonstrate non-obviousness. Specifically, § 103(a) assumes that no single prior art reference discloses every limitation recited in the claims. Using applicant's proposed criteria of obviousness, no reference could ever demonstrate obviousness, unless it in fact anticipated the claimed subject matter. In fact, according to applicant's logic, any reference which failed to make the claimed combination would in fact be evidence of the non-obviousness of the claimed invention. This is simply not the state of the law.

Rather, the inquiry required under § 103(a) is that "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art[,] then a patent on that subject matter cannot be obtained. Section 103(a) does not mention anything about how long the elements had been available to prior art practitioners. While, the age of the references

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may be of relevance when looking to secondary considerations of obviousness (e.g., solving a long-felt, but unsolved need), the relative age of the cited references cannot be considered evidence of non-obviousness, absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977).

With respect to the assertion that only through hindsight would the artisan of ordinary skill have made the combination of references made in the rejection, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case applicant's claims recite an assembly of elements known to be useful in the preparation of fucosylated products. As discussed above, and in the previous office action, the artisan of ordinary skill, recognizing solely from the prior art that the claimed combinations of enzymes were suitable in the preparation of fucosylated oligosaccharides, clearly would have

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been motivated to have assembled the claimed ingredients into a single composition. The rejections of record are therefore properly maintained.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

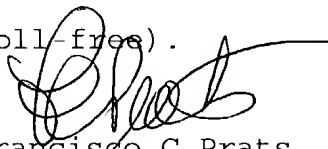
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 571-272-0921. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Francisco C Prats  
Primary Examiner  
Art Unit 1651

FCP